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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,257	12/21/2001	Peter Krulevitch	IL-10580	6642

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EXAMINER	
BEISNER, WILLIAM H	

ART UNIT	PAPER NUMBER
1744	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,257	KRULEVITCH ET AL.	
	Examiner	Art Unit	
	William H. Beisner	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krulevitch et al.(US 5,985,217 or US 6,319,474) in view of Wilding et al.(US 6,184,029).

The references of Krulevitch et al. disclose a microfabricated biopsy/genetic analysis instrument, comprising: a cutter section (35), a specimen chamber (34) located adjacent said cutter section, a specimen treatment section (40) located adjacent said specimen chamber.

While the references Krulevitch et al. disclose that the device includes microchannels for delivering chemicals for treating the specimen, claims 1 and 16 differ by reciting that the device includes a PCR reaction chamber section "that is integral with said specimen treatment section or abuts" the specimen treatment chamber.

The reference of Wilding et al. discloses that it is known in the art to combine microfabricated sample preparation device with microfabricated analyte detection and/or microfabricated polynucleotide amplification (See column 3, lines 33-43). The reference of Wilding et al. discloses a microfabricated device that includes a PCR reaction chamber (See Figures 11A and 11B). The reference also discloses that a number of sample sources can be used in the device (See column 22, lines 17-27).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to communicate a PCR reaction chamber with the specimen treatment section for the known and expected result of providing a means recognized in the art for analyzing the sample after being treated and/or processed in the specimen treatment section. As shown in Figures 11A and 11b of the reference of Wilding et al., communication of the PCR chamber with the sample preparation chamber would be provided using a microchannel. Provision of a PCR reaction chamber allows verification of the specimen by amplification and

detection of the nucleic acid contained in the sample tissue. Nucleic acid verification would not be capable with the optical system currently disclosed by the references of Krulevitch et al.

With respect to claims 2-4, the references of Krulevitch et al. disclose cutting edge (35) and tapered opening (34) made of a silicon substrate.

With respect to claims 5, 6 and 9, the references of Krulevitch et al. disclose the use of "another" member (32) made of glass. The reference of Wilding et al. also discloses the use of glass as a substrate (See column 8, lines 38-53). As a result, it would have been obvious to provide the microchannels required for adding reagents and/or moving the sample within the device and PCR reaction chamber within substrate (32) of the Krulevitch et al. reference for the known and expected result of using a single substrate for providing the microfluidic channels and chambers suggested by the combination of the references discussed above since the reference of Wilding et al. discloses a similar means of manufacture as that disclosed by the primary references.

With respect to claim 7, the references of Krulevitch et al. disclose a fluid inlet (39) and microchannel (40).

With respect to claims 8 and 19, the references of Krulevitch et al. disclose an optical analysis device (47).

With respect to claim 10, the reference of Wilding et al. discloses that the PCR reaction chamber includes an outlet for post-amplification detection.

With respect to claims 11, 12 and 18, as shown in Figures 11a and 11b of the Wilding et al. reference, the PCR reaction chamber (222A) has a width or cross-section that is greater than the channels and/or chambers upstream to the PCR reaction chamber.

With respect to claims 13 and 14, whether or not the PCR treatment chamber is integral or separate from the sample preparation chamber would have been merely an obvious matter in design choice since the step of making an element integral or separable is not deemed to be a patentably distinct improvement.

With respect to claim 15, the references of Krulevitch et al. disclose both the cutter section (35) and the specimen holding or treatment section formed on the same substrate (31).

With respect to claim 17, whether the treatment zones of the device are formed on a single substrate or plural substrates would have been an obvious matter in design choice based merely on the means for manufacture of the device. Etching would involve two substrates while machining could produce the device on a single substrate.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 5,985,217 in view of Wilding et al.(US 6,184,029). Claims 1-15 of U.S. Patent 5,985,217 encompass a

microfabricated biopsy/genetic analysis instrument, comprising: a cutter section, a specimen chamber located adjacent said cutter section, a specimen treatment section located adjacent said specimen chamber.

While the claims disclose that the device includes microchannels for delivering chemicals for treating the specimen, claims 1 and 16 differ by reciting that the device includes a PCR reaction chamber section "that is integral with said specimen treatment section or abuts" the specimen treatment chamber.

The reference of Wilding et al. discloses that it is known in the art to combine microfabricated sample preparation device with microfabricated analyte detection and/or microfabricated polynucleotide amplification (See column 3, lines 33-43). The reference of Wilding et al. discloses a microfabricated device that includes a PCR reaction chamber (See Figures 11A and 11B). The reference also discloses that a number of sample sources can be used in the device (See column 22, lines 17-27).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to communicate a PCR reaction chamber with the specimen treatment section for the known and expected result of providing a means recognized in the art for analyzing the sample after being treated and/or processed in the specimen treatment section. As shown in Figures 11A and 11b of the reference of Wilding et al., communication of the PCR chamber with the sample preparation chamber would be provided using a microchannel. Provision of a PCR reaction chamber allows verification of the specimen by amplification and detection of the nucleic acid contained in the sample tissue. Nucleic acid verification would not be capable with the optical system currently disclosed by the references of Krulevitch et al.

With respect to claim 10, the reference of Wilding et al. discloses that the PCR reaction chamber includes an outlet for post-amplification detection.

With respect to claims 11, 12 and 18, as shown in Figures 11a and 11b of the Wilding et al. reference, the PCR reaction chamber (222A) has a width or cross-section that is greater than the channels and/or chambers upstream to the PCR reaction chamber.

With respect to claims 13 and 14, whether or not the PCR treatment chamber is integral or separate from the sample preparation chamber would have been merely an obvious matter in design choice since the step of making an element integral or separable is not deemed to be a patentably distinct improvement.

With respect to claim 15, the references of Krulevitch et al. disclose both the cutter section (35) and the specimen holding or treatment section formed on the same substrate (31).

With respect to claim 17, whether the treatment zones of the device are formed on a single substrate or plural substrates would have been an obvious matter in design choice based merely on the means for manufacture of the device. Etching would involve two substrates while machining could produce the device on a single substrate.

6. Claims 1-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17 of U.S. Patent No. 6,319,474 in view of Wilding et al.(US 6,184,029). Claims 1-19 are obvious over claim 17 and the reference of Wilding et al. for the same reasons as set forth with respect to the combination of Claims 1-15 of U.S. Patent '217 and Wilding et al. set forth above.

Response to Arguments

7. Applicant's arguments filed 30 Jan. 2004 have been fully considered but they are not persuasive.

Applicants argue that it would not be obvious to combine the chamber 198a and 198b and/or chamber 22A of the Wilding et al. reference with either of the Krulevitch et al. references and any such combination would still not show the invention defined by Applicants' amended claims.

i) Applicants argue that "None of the three references show or suggest Applicant's claim elements. Since none of the three references show Applicant's claim elements, there can be no combination of the references that show Applicant's claim elements".

ii) Applicants argue "there would not be a reasonable expectation of success of any combination of the three references. There is no teaching of how the structure in the Wilding et al. reference would be combined with the structure in the Krulevitch et al. references".

iii) Applicants argue the examiner has employed "impermissible hindsight" when combining any of the references of Krulevitch et al. with the reference of Wilding et al.

In response to argument i) above, if Applicants' position is that none of the three references, individually, show Applicants' claim elements, the Examiner agrees with this statement. For this reason, the Examiner was required to make an obviousness rejection under 35 USC 103 rather than an anticipatory rejection under 35 USC 102. However, if Applicants' position is that the combination of either of the references of Krulevitch et al. with the reference of Wilding et al. does not show Applicants' claim elements, the Examiner disagrees. As stated in the 35 USC 103 rejection above, the references of Krulevitch et al. disclose all of the claimed

elements except for a PCR chamber section "that is integral with said specimen treatment section or abuts" the specimen treatment chamber. The reference of Wilding et al. was cited as a prior art teaching that disclosed that it is known in the art to provide a nucleic acid amplification chamber (PCR) in communication with a sample preparation section on a microfluidic-type device. The nucleic acid amplification chamber is provided in communication with the sample preparation section using a "microchannel". This type of communication is considered to meet the instant claim language "integral with" since the instant specification at paragraph [0010] and Figures 2-4 show the PCR sections (22,52) in fluid communication with the sample treatment via microchannel (30,54). In view of the combination of the references as discussed previously, the Examiner is of the position that the three references do show Applicants' claim elements.

In response to argument ii) above, it appears from Applicants' comments that the references are required to specifically instruct one of ordinary skill in the art how to mechanically combine the device of Wilding et al. with the device of either of the Krulevitch et al. references. Note the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In this case, both of the primary references of Krulevitch et al. disclose microfluidic sample preparation devices. Both of these references discloses the use of microchannels (40) for contacting a fluid with the sample to be treated. The secondary reference of Wilding et al. is also within the field of microfluidic devices. Specifically, the disclosure of Wilding et al. encompasses sample preparation in

combination with sample amplification and/or detection in chambers connected serially to the sample preparation channel using microchannels for fluid communication between the chambers. The Examiner is of the position that one of ordinary skill in the art presented with the disclosures of Krulevitch et al. and Wilding et al. before them would have recognized that the sample preparation chamber of Krulevitch et al. can be modified to include a microchannel connecting the sample preparation chamber with a sample amplification chamber as suggested by the reference of Wilding et al. Especially since both references are within the field of microfluidic sample preparation and detection.

In response to argument iii) above, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As discussed above, only knowledge which was within the level of ordinary skill in the art at the time the invention was made was employed to support the combination of the claim elements.

With respect to the obviousness-type double patenting rejections of record, the combination of the reference of Wilding et al. with the claims of the Krulevitch et al. reference is deemed proper for the same reasons as set forth above with respect to the 35 USC 103 rejections of record.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 571-272-1281. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

William H. Beisner
Primary Examiner
Art Unit 1744

WHB